3128

Special Feature

Analysis of SBIR phase I and phase II review results at the National Institutes of Health

KIRT J. VENER,[1] AND BEVERLY M. CALKINS

National Institute of Arthritis, and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA, and Jonsson Comprehensive Cancer Center, University of California, Los Angeles, Los Angeles, California 90024.

ABSTRACT A cohort **of phase I and phase II summary statements for the SBIR grant applications was evaluated to determine the strengths and weaknesses in approved and disapproved applications. An analysis of outcome variables (disapproval or unfunded status) was examined with respect to exposure variables (strengths or shortcomings). Logistic regression models were developed for comparisons to measure the predictive value of 'shortcomings and strengths to the outcomes. Disapproved phase I results were compared with an earlier 1985 study. Although the magnitude of the frequencies of shortcomings was greater in the present study, the relative rankings within shortcoming class were more alike than different. Also, the frequencies of shortcomings were, with one exception, not significantly different in the two studies. Differences in the summary statement review may have accounted for some differences observed between the 1985 data and results of the present study. Comparisons of Approved/Disapproved and Approved-Unfunded/Funded yielded the following observations. For phase I applicants, a lack of a clearly stated, testable hypothesis, a poorly qualified or described investigative team, and inadequate methodological approaches contributed significantly (in that order) to a rating of disapproval. A critical flaw for phase II proposals was failure to accomplish objectives of the phase I study. Methodological issues also dominate the distinctions in both comparison groups. A clear result of the data presented here and that published previously is that SBIR applicants need continuing assistance to improve the chances of their success. These results should serve as a guide to assist NIH staff as they provide information to prospective applicants focusing on key elements of the application. A continuing review of the SBIR program would be helpful to evaluate the quality of the submitted science.-Vener, K. J.; Calkins, B. M. Analysis of SBIR phase I and phase II** review **results at the National Institutes of Health. *FASEB J. 5: 2640-2644;* 1991.**

Key Words: *commerce . National Institutes of Health . professional competence . research design-standards . research support-economics . United States*

THE SMALL BUSINESS INNOVATION Development Act of 1982 (Public Law 97-219) was signed into law by President Reagan on July 22, 1982 (1).[2] The purposes of the legislation were fourfold: *1*) to stimulate technological innovation; 2) to use small business to meet federal research and development needs; 3) to foster and encourage participation by minority and disadvantaged persons in technological innovation; and, 4) to increase private sector commercialization innovations from federal research and development. Federal agencies whose extramural research and development budgets were in excess of $100 million were required to participate in the Small Business Innovation Research (SBIR)[3] program. To facilitate implementation of the program in all agencies, the percentage of an agency's R&D budget to be dedicated to the effort started at 0.2% in the first year and rose gradually to the present level of 1.25%.

Two standard award instruments are used to support SBIR: the grant and the contract. The grant instrument supports investigator-initiated research. The proposal submitted by the investigator may or may not be in response to a call for applications in a specific scientific area. In the contract mechanism, the one making the offer submits a proposal in response to a specific solicitation by an agency. This mechanism allows much less flexibility for the person making the offer. Because this manuscript deals with the grant mechanism of SBIR support at the National Institutes of Health (NIH), the contract aspect of the SBIR program will not be discussed.

Two phases of the SBIR grant program are supported with federal funds from the budget set aside. Phase I is designed to establish the technical merit and feasibility of the proposed research. The duration of phase I is 6 months at a maximum cost of $50,000 with no cost time extensions possible. The objective of phase II, the duration of which is generally 2 years and funding level of up to $500,000, is to continue research and development of phase I work. Separate applications are required for these two phases of support, with phase II funding based on the results of phase I work and on the technical and scientific merit of the phase II proposal. Phase I applications are given the activity code of R43 whereas phase II applications are designated R44s. Procedures for the solicitation, receipt, review, and award are similar to the regular research grants program at NIH and are described elsewhere (2, 3).

[1] This article was written by Kirt J. Vener in his private capacity. No official support or endorsement by the National Institutes of Health or the Public Health Service is intended or should be inferred.

[2] A paraphrase definition of a small business is that it is a for-profit entity, located in the U.S., 51% owned by U.S. citizens, has less than 500 employees and must meet the regulatory requirements of 13 CFR Part 121.

[3] Abbreviations: SBIR, Small Business Innovation Research; NIH, National Institutes of Health, PHS, Public Health Service.

Interest in the SBIR program remains high among members of the small business community. Since inception of the program in fiscal year 1983, and through the end of fiscal year 1988, almost $1.4 billion has been awarded by all participating federal agencies. In response to a total of 78 SBIR solicitations issued by the 12 federal departments participating in the SBIR program, those agencies received 70,066 phase I and 3976 phase II proposals resulting in 9229 phase I and 2788 phase II awards. **Figure 1** shows the total number of awards issued and the total dollar amount by fiscal year.

NIH SBIR APPLICATION AND AWARD HISTORY

The application and award history of the SBIR program at the NIH parallels government-wide trends and is shown in **Fig. 2** and **Fig. 3,** respectively. After increasing for the first 4 years of the program, the number of phase I (Fig. 2) submissions plateaued at approximately 1400. -The percentage of approved (or funding eligible) applications funded in fiscal year 1984 reached a peak of 68.5%. This percentage declined to about 33.6% in 1988. As more phase II (Fig. 3) proposals were funded, a larger proportion of the overall SBIR budget was utilized for phase II studies (data not shown). The percentage of eligible R44 applications funded in fiscal year 1988 was 51.8%. Sample titles of phase I and phase II grants are shown in Table 1 and Table 2.

RATIONALE FOR THIS REPORT

Using the summary statements resulting from review of the SBIR proposals, there were four objectives to the present analysis. The first objective was to determine whether the shortcomings described in Table 3 are occurring with the same frequency 3 years later in disapproved applications. The second objective was not only to assess phase I shortcomings, as was done for fiscal year 1983 proposals, but to extend the analysis to include: 1) an assessment of strengths of proposals; 2) a comparison of approved and disapproved proposals, and among approved proposals; and 3) a comparison of proposals that were funded and unfunded. The third objective was to describe for a group of phase II proposals the shortcomings and strengths articulated in their corresponding summary statements. Thk final objective is to provide information to the NIH extramural staff so that they may help applicants in preparing proposals by, among other things, pointing out pitfalls to be avoided in the proposal preparation process.

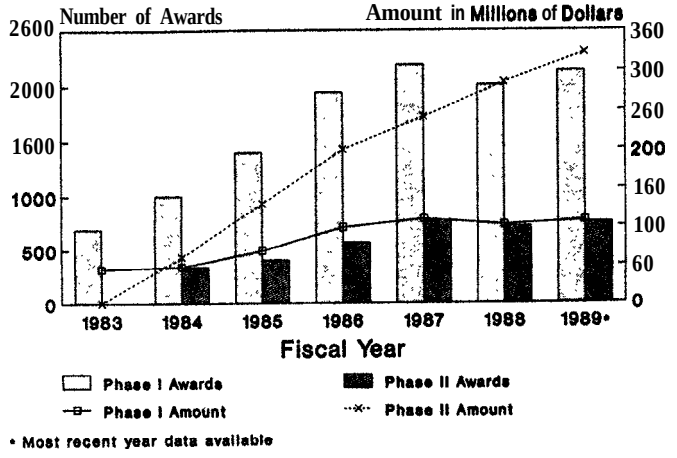

Figure 1. SBIR awards: number and amount for **all** Federal agencies. Source: SBA, July 1990.

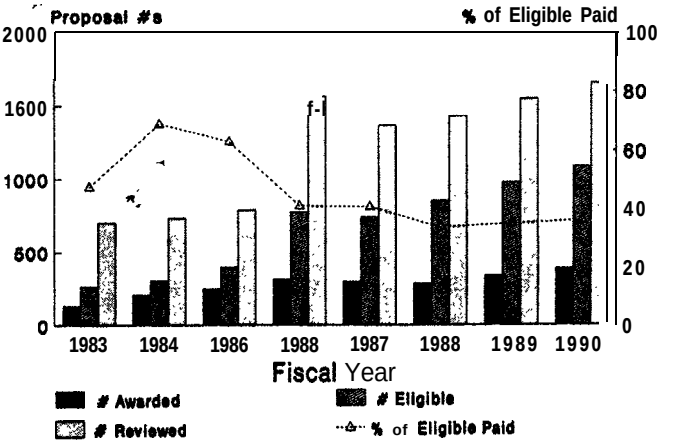

Figure 2. Phase I SBIR history (R43 Application and Award Summary), National Institutes of Health. Source: Statistical Analysis and Evaluation Section, DRG, NIH.

MATERIALS AND METHODS

Table 3 describes characteristics of the data set. Phase I applications were drawn from the October 1986 Council (N = 407) and phase II proposals were selected from the October 1986, October 1987, and January 1988 Council rounds (N = 265). For phase I applications the summary statements came from a series of ad hoc study sections convened to review SBIR proposals.

Shortcomings and strengths were divided into five different classes based on similar summary statement analyses by other investigators (4). These classes are: class I, The Nature of the Research Problem; class II, The Experimental Approach; class III, The Investigators; class IV, Requirements of the SBIR Program; and class V, Other.

Data analysis was performed using the EPIINFO software developed by the Centers for Disease Control in Atlanta. Appropriate controls were used to assess inter- and intraindividual rater variation. A logistic regression model (5) was used to determine the contributions of strengths or weaknesses to the two comparisons: disapproval vs. approval and approved-unfunded vs. approved-funded.

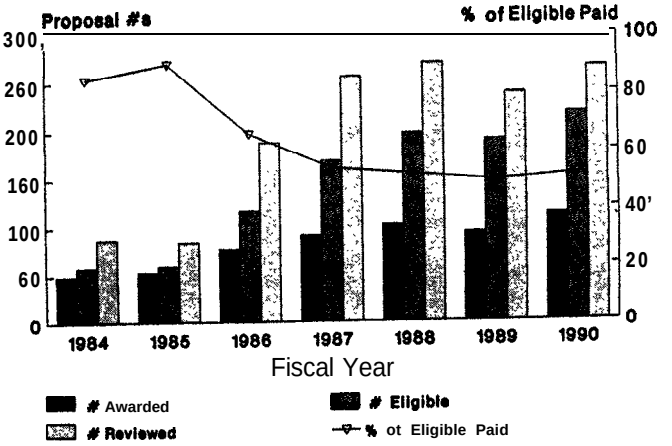

Figure 3. Phase II SBIR history (R44 Application and Award Summary), National Institutes of Health. Source: Statistical Analysis and Evaluation Section, DRG, NIH.

TABLE 1. *Examples of SBIR phase I grants*[a]

- Computerized nutrition program for senior citizens
- Rapid diagnostic tests for adenoviruses
- Drugs that inhibit pruritis
- Positron emission tomography for clinical use
- Anticalculus agents
- Laser fragmentation of biliary stones
- Carcinogenesis information for environmental substances
- Stereometric optic disk analysis
- Novel probes for efficient genetic disease diagnosis
- Audiovisuals for blood pressure training and testing
- Automated testing for neurological deficits
- Flow cytometry — Improving cost effectiveness

[a] *Source:* Department of Health and Human Services.

RESULTS AND DISCUSSION

Phase I data

Comparison of 1983 and 1986 data

Table 3 provides a comparison of the data, published in 1985 (1983 Council actions) and the new data reported for this study (1986 Council actions) for the phase I applications. A chi-squared analysis was performed on the occurrence frequencies for each cohort for each shortcoming. A statistical difference in the relative frequencies is denoted by a triangle after the 1986 cohort column. In the first group of shortcomings (the experimental problem), without exception the frequencies of occurrence of each shortcoming were significantly greater in the 1986 cohort compared with the earlier, 1983 cohort. Within the problem category (class I) and for each cohort, shortcoining 1 (a poor hypothesis) was the most frequent observation. In the approach section (class II), the general trend is the same as in class I; that is, the proportion with class II shortcomings in the most recent study is significantly greater than in the earlier study. Exceptions to that observation are shortcomings 8 and 9 (controls and appropriate material) where significant variation did not occur. Shortcoming 5 (weakness in study design) is a prominent weakness in the second study along with shortcoming 4 (poor description of approach).

In the class III category, investigator, there was no difference in the proportion of shortcomings 11, 12, and 13 between 1983 and 1986. However, shortcoming 14 (poorly documented collaborative arrangements) was more frequent in the 1986 group. In the final class of shortcomings (SBIR requirements), the limited potential for commercial application (#15) was twice as frequent in the 1986 cohort. The frequency of shortcomings in technological innovation (#16) and the magnitude of the effort (#17) were the same in both cohorts.

Given the general trend of the comparisons in Table 3, there are several interesting points. First, in the approach section shortcoming #5 (poor study design) is significantly greater in the 1986 review results compared with the 1983 study. There are several possible explanations for differences in the results of the two studies. These include usine external examiners to review the summary statements; differences in composition of the study sections; and different executive secretaries. In the investigator class of shortcomings (shortcomings 11, 12, and 13) failure to demonstrate significant differences suggests that the quality of the investigators in the 1986 group compared with the 1983 group is about the same. Under SBIR Requirements, although the potential for commercial application seems to be somewhat less in 1986 than in 1983, the technological innovation seems to have improved.

Analysis of the 1986 phase Z and the phase ZZ applications

Table 4 describes characteristics of the application data used for analysis. EPIINFO permitted subset analysis of the importance of the different variables (i.e., shortcomings and strengths) in arriving at a particular outcome (i.e., disapproval, approval-unfunded, approval-funded). Table 5 and Table 6 display those variables which significantly contributed to one of the outcomes for the approved-unfunded vs. approved-funded comparison for the phase I (Table 5) and phase II (Table 6) applications. Results of the disapproval vs. approval comparisons were similar to those of the unfunded vs. funded data. Where appropriate, differences between the comparison groups will be noted.

Table 5 reflects the S-S comparison for phase I approved-unfunded and approved-funded applications. Using a logistic regression model (with shortcomings only), the most significant shortcomings, the *absence* of which contributed to funded status, were: collaboration is needed, hypothesis is poor, lack of familiarity with the literature, unsuitable methods, poor study design, limited commercial application, and more complex than appreciated. Similarly, using a logistic regression model (with strengths only), presence of the following strengths were predictive of funding. These were: methods in place, proposal is well thought out, a need exists, and good commercial potential. The combined regression model indicates that the absence of six shortcomings are predictive of funded status (poor hypothesis, excessive complexity, unsuitable methods, collaboration is needed, lack of familiarity with the literature, and limited commercial application). Furthermore, three strengths are most predictive of being funded (methods in place, a need exists, and good commercial potential). In addition, adequate facilities were important in the decision between approval and disapproval.

Table 6 reflects the S-S comparisons for phase II approved-unfunded and approved-funded applications. Using a logistic regression model (with shortcomings only), the presence of four of the shortcomings were found to be predictive of unfunded status (unmet phase I objectives, poor study design, little innovation, and inadequate objectives and methods). Using a logistic regression model (with strengths only), absence of four of the strengths was found to be predictive of nonfunding. These were: defined collaborative

TABLE 2. *Examples of SBIR phase II grants*[a]

- Fall injury prevention system for the aged
- Control of Schistosomiasis by rotifer emissions
- Sensitive probe for intraoperative bone scanning
- A new large-scale affinity separation technique
- An acoustic body volumeter
- A periodontal temperature probe
- Pill usage chronolog and reminder
- An instrument for in vitro cytometry
- Development of tactile paper for low vision
- Correlation of dynamic molecular shape with activity
- An automated hematology microscope
- Rehabilitative software for head trauma victims

[a] Source: Department of Health and Human Services.

TABLE 3. *Shortcomings found* in *disapproved SBIR, phase I Proposals reviewed for fiscal year 1983 and 1986 action*

No.	Shortcoming	% of occurrence 1983[a]	1986[b]
	Class I: problem		
1	The proposed research is based on a hypothesis that rests on insufficient evidence, is doubtful, or is unsound	44.3	72.0'
2	The problem is more complex than the investigtaor appears to realize	15.3	39.6'
3	The problem is of insufficient importance to warrant approval	10.8	38.5'
	Class II: approach		
4	The description of the approach is too nebulous, diffuse, and lacking in clarity and technical information to permit adequate evaluation	48.6	70.3'
5	The overall design of the study has not been carefully thought out and developed	28.1	78.0'
6	Facilities or resources are not described or are inadequate	10.5	31.3"
7	The statistical aspects of the approach have not been given sufficient consideration	7.7	18.1'
8	Controls are either inadequately conceived or inadequately described	6.8	14.8
9	'The material the investigator proposes to use is unsuited to the objectives of the study	5.4	8.2
10	The proposed tests, or methods or scientific procedures are unsuited or unrelated to the stated objective	4.8	20.9'
	Class III: investigator		
11	The investigator does not have adequate experience or training, or both, for this research	44.4	37.4
12	The investigator appears to be unfamiliar with pertinent methods or literature, or both	40.6	33.0
13	The investigator needs more liaison with colleagues in this field or collateral fields	10.9	18.1
14	Collaborative arrangements are not described or not documented	8.8	19.8'
	Class IV: SBIR requirements		
15	There is limited potential for commercial application	23.0	56.6'
16	There is little technological innovation	23.0	23.6
17	The magnitude of the proposed effort is unrealistic for the amount of time allocated for phase I work	15.6	15.4
18	The cost of performing the phase I work exceeds the SBIR guidelines	6.0	0.0'

[a] $N = 356$. [b] $N = 182$. [c] X^2 comparison significant at <0.05.

arrangements, well thought out, well designed, and accomplished phase I objectives. In the combined regression model the characteristics most predictive of being funded are the absence of two shortcomings (failure to achieve phase I objectives and inadequate objective and methods), and the presence of two strengths (the proposal is well thought out and it is well designed). Shortcomings related to the approaches used and the SBIR requirements dominate the results. The latter is also the case for disapproved vs. approved phase II applications.

When comparing Table 6 with Table 5, investigator difficulties seem less problematic in phase II than in phase I. As with other shortcomings and strengths, the latter is likely due to the removal of less qualified applicants during the phase I review.

SUMMARY AND CONCLUSIONS

From the preceding description and data discussion it is clear that *1*) mechanics of the SBIR program are working, and *2*) a continuing effort must be made to develop the grantsmanship skills of the SBIR applicants. That the SBIR program has had a positive effect on the overall mission of the Public Health Service (PHS) was pointed out in an internal 1988 PHS report listing several positive outcomes from the PHS SBIR activity. First, the SBIR program has permitted development of instrumentation which was difficult to support under conventional or traditional grant support mechanisms. Second, SBIR activities have permitted applied research projects to proceed, providing a modicum of balance in program needs. Third, a whole new spectrum of

TABLE 4. *SBZR data set characteristics"*

Characteristic	Phase I		Phase II	
	Approved	Disapproved	Approved	Disapproved
Total	225	182	181	84
Number funded	90 (40%)	—	79 (44%)	—
Number amended	27 (12%)	31 (17%)	11 (6%)	25 (30%)
Bachelors (all)	19 (8%)	31 (17%)	10 (6%)	13 (16%)
Masters (all)	28 (12%)	37 (20%)	14 (7%)	9 (11%)
Ph.D.	149 (66%)	87 (48%)	117 (65%)	41 (49%)
M.D.	14 (6%)	9 (5%)	11 (9%)	8 (10%)
Other professional	5 (2%)	10 (6%)	8 (4%)	4 (5%)
No degree identified	10 (4%)	8 (4%)	21 (12%)	9 (11%)

"Phase I: October 1986 Council (N = 407); Phase II: October 1986, 1987, and January 1988 (N = 265).

TABLE 5. *A* listing *of shortcomings and strengths contributing to funding (compared to unjunded) in phase I applications*

Shortcomings	Strengths
Poor hypothesis"	Methodologies in place"
Collaboration is needed'	Well thought out
Poor study design	Need exists[a]
Unsuitable methods'	Good commercial potential"
Unfamiliar with literature'	
Poor commercial potential	
Overly complex	

"Absence of these attributes (when shortcomings) or presence (when strengths) are predictive of funded status by logistic regression when shortcomings and strengths are combined in the model.

resources has been made available in both the intellectual base of the applicants and their physical facilities. Fourth, important new relationships have been developed between the SBIR applicants and the university colleagues who collaborate on many of the projects. Finally, because conventional granting mechanisms do not permit product development, the SBIR program has provided for support of development projects that may never have come to the attention of the awarding agencies.

However, an issue yet to be resolved is the suggestion that there is increasing difficulty in clinical testing of devices because of liability issues (William Partridge, personal communication). The expanding magnitude of medical products liability litigation, which results in part from a standard of absolute liability, has already forced some manufacturers to remove their products from the marketplace (6). This trend could increasingly affect grantees supported by the federal SBIR program, although it is possible that the buyout of SBIR grantees by large companies that are better able to cope with product liability issues would permit technology transfer to continue. In 1986 the National Childhood Vaccine Act (P.L. 99-660) became law. This legislation provided for the compensation of patients who experienced in adverse reaction to a vaccine product. It is conceivable that a similar program may be necessary to provide an additional measure of protection for SBIR medical device manufacturers and their clinical colleagues.

A clear result of the data presented here and that published previously (3) is that SBIR applicants need continuing assistance to improve the chances of their success. These results should serve as a guide to assist NIH staff as they provide information to prospective applicants focusing on key elements of the application. Prospective applicants are provided with some "DOS and Don'ts" to consider during the process of application in **Table 7 and Table 8.** A continuing review of the SBIR program would be helpful to determine if the quality of the submitted science can be improved. FJ

TABLE 6. *A listing of shortcomings and strengths contributing to funding (compared to unfunded) in phase II applications*

Shortcomings	Strengths
Unmet phase I objectives'	Defined collaboration
Little innovation	Well thought out"
Poor study design	Well designed*
Inadequate methodology"	Achieved phase I objective

"Absence of these attributes (when shortcomings) or presence (when strengths) are predictive of funded status by logistic regression when shortcomings and strengths are combined in the model.

TABLE 7. DOS *and don'ts for phase I applicants*

Dos

- Make sure methodologies are in place
- Carefully think through your proposal and anticipate questions
- Clearly describe the available facilities and resources
- Document that a need exists
- Document the commercial potential
- Assume that you must educate and persuade the review group of the importance of your work

Don'ts

- Don't submit your application in haste.
- Don't underestimate the importance of a clearly stated hypothesis; you are submitting a research grant application.
- Don't be reluctant to state the importance of your proposal in terms of health care benefit, cost savings or scientific value.
- Don't skimp *on* citing up to date and relevant literature pertaining to your hypothesis and your work,
- Don't underestimate the complexity of your project.
- Don't be reluctant to seek expert consultation to bolster your. project.

TABLE 8. *Dos and Don'ts for Phase II Applicants*

Dos

- Describe how the phase I objectives were met
- Carefully think through your proposal and anticipate questions
- Clearly describe the available facilities and resources
- Spend time'carefully designing your studies.
- Assume that you must educate and persuade the review group of the importance of your work.

Don'ts

- Don't skimp on the objectives and the methods you will use to accomplish those objectives.
- Don't understate the technological innovation of your work
- Don't underestimate the complexity of your project; demonstrate that you understand the complexity and are in a position to deal with it.
- Don't submit your application in haste.

The authors would like to thank the following individuals for their technical assistance in preparing this manuscript: Mr. David Benoir, Mr. Jeff Caffey, Ms. Joan Fredericks, Dr. Francis Kendricks, Mr. Robert Moore, and Ms. Hillary Shein. The authors would also like to thank Drs. Norman Braveman, Tommy Broadwater, and Paul Parakkal and Ms. Lily Engstrom for their helpful comments. This project was supported in part by project no. NIH 88-313 from the 1% evaluation set aside.

REFERENCES

1. Anonymous. (1990) Small Business Innovation Development Act: seventh year results, Small Business Administration, Washington, D.C.
2. Murphy, D. G., and Dean, D. J. (1984) Application and review procedures for the NIH Small Business Innovation Research Program. *Institute Insight* March 1-12
3. Vener, K. J. (1985) National Institutes of Health phase I, Small Business Innovation Research applications: fiscal year 1983 results. *Federation Proc. 44, 2679-2684*
4. Allen, E. M. (1960) Why are research grant applications disapproved? *Science* 132, 1532-1534
5. Kleinbaum, D. G., Kupper, I., and Morgenstern, H. (1982) *Epidemiologic Research.* Lifetime Learning Publications, Belmont, California
6. Price, J. M. (1987) The liabilities and consequences of medical device development. *J. Biomed. Materials Res.* (Al suppl.): 35-58

Special Feature

Analysis of SBIR phase I and phase II review results at the National Institutes of Health

KIRT J. VENER,' AND BEVERLY M. CALKINS

National Institute of Arthritis, and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA; and Jonsson Comprehensive Cancer Center, University of California, Los Angeles, Los Angeles, California 90024.

ABSTRACT **A cohort of phase I and phase II summary statements for the SBIR grant applications was evaluated to determine the strengths and weaknesses in approved and disapproved applications. An analysis of outcome variables (disapproval or unfunded status) was examined with respect to exposure variables (strengths or shortcomings). Logistic regression models were developed for comparisons to measure the predictive value of shortcomings and strengths to the outcomes. Disapproved phase I results were compared with an earlier 1985 study. Although the magnitude of the frequencies of shortcomings was greater in the present study, the relative rankings within shortcoming class were more alike than different. Also, the frequencies of shortcomings were, with one exception, not significantly different in the two studies. Differences in the summary statement review may have accounted for some differences observed between the 1985 data and results of the present study. Comparisons of Approved/Disapproved and Approved-Unfunded/Funded yielded the following observations. For phase I applicants, a lack of a clearly stated, testable hypothesis, a poorly qualified or described investigative team, and inadequate methodological approaches contributed significantly (in that order) to a rating of disapproval. A critical flaw for phase II proposals was failure to accomplish objectives of the phase I study. Methodological issues also dominate the distinctions in both comparison groups. A clear result of the data presented here and that published previously is that SBIR applicants need continuing assistance to improve the chances of their success. These results should serve as a guide to assist NIH staff as they provide information to prospective applicants focusing on key elements of the application. A continuing review of the SBIR program would be helpful to evaluate the quality of the submitted science.-Vener, K. J.; Calkins, B. M. Analysis of SBIR phase I and phase II review results at the National Institutes of Health.** *FASEB J. 5: 2640-2644;* **1991.**

Key *Words: commerce • National Institutes of Health • professional competence • research design-standards • research support-economics • United States*

THE SMALL BUSINESS INNOVATION Development Act of 1982 (Public Law 97-219) was signed into law by President Reagan on July 22, 1982 (1).[2] The purposes of the legislation were fourfold: *1*) to stimulate technological innovation; 2) to use small business to meet federal research and development needs; 3) to foster and encourage participation by minority and disadvantaged persons in technological innovation; and 4) to increase private sector commercialization innovations from federal research and development. Federal agencies whose extramural research and development budgets were in excess of $100 million were required to participate in the Small Business Innovation Research (SBIR)[3] program. To facilitate implementation of the program in all agencies, the percentage of an agency's R&D budget to be dedicated to the effort started at 0.2% in the first year and rose gradually to the present level of 1.25%.

Two standard award instruments are used to support SBIR: the grant and the contract. The grant instrument supports investigator-initiated research. The proposal submitted by the investigator may or may not be in response to a call for applications in a specific scientific area. In the contract mechanism, the one making the offer submits a proposal in response to a specific solicitation by an agency. This mechanism allows much less flexibility for the person making the offer. Because this manuscript deals with the grant mechanism of SBIR support at the National Institutes of Health (NIH), the contract aspect of the SBIR program will not be discussed.

Two phases of the SBIR grant program are supported with federal funds from the budget set aside. Phase I is designed to establish the technical merit and feasibility of the proposed research. The duration of phase I is 6 months at a maximum cost of $50,000 with no cost time extensions possible. The objective of phase II, the duration of which is generally 2 years and funding level of up to $500,000, is to continue research and development of phase I work. Separate applications are required for these two phases of support, with phase II funding based on the results of phase I work and on the technical and scientific merit of the phase II proposal. Phase I applications are given the activity code of R43 whereas phase II applications are designated R44s. Procedures for the solicitation, receipt, review, and award are similar to the regular research grants program at NIH and are described elsewhere (2, 3).

'This article was written by Kirt J. Vener in his private capacity. No official support or endorsement by the National Institutes of Health or the Public Health Service is intended or should be inferred.

[2]A paraphrase definition of a small business is that it is a for-profit entity, located in the U.S., 51% owned by U.S. citizens, has less than 500 employees and must meet the regulatory requirements of 13 CFR Part 121.

[3]Abbreviations: SBIR, Small Business Innovation Research; NIH, National Institutes of Health, PHS, Public Health Service.

Interest in the SBIR program remains high among members of the small business community. Since inception of the program in fiscal year 1983, and through the end of fiscal year 1988, almost $1.4 billion has been awarded by all participating federal agencies. In response to a total of 78 SBIR solicitations issued by the 12 federal departments participating in the SBIR program, those agencies received 70,066 phase I and 3976 phase II proposals resulting in 9229 phase I and 2788 phase II awards, Figure 1 shows the total number of awards issued and the total dollar amount by fiscal year.

NIH SBIR APPLICATION AND AWARD HISTORY

The application and award history of the SBIR program at the NIH parallels government-wide trends and is shown in Fig. 2 and Fig. 3, respectively. After increasing for the first 4 years of the program, the number of phase I (Fig. 2) submissions piateaued at approximately 1400. -The percentage of approved (or funding eligible) applications funded in fiscal year 1984 reached a peak of 68.5%. This percentage declined to about 33.6% in 1988. As more phase II (Fig. 3) proposals were funded, a larger proportion of the overall SBIR budget was utilized for phase II studies (data not shown). The percentage of eligible R44 applications funded in fiscal year 1988 was 51.8%. Sample titles of phase I and phase II grants are shown in Table 1 and Table 2.

RATIONALE FOR THIS REPORT

Using the summary statements resulting from review of the SBIR proposals, there were four objectives to the present analysis. The first objective was to determine whether the shortcomings described in Table 3 are occurring with the same frequency 3 years later in disapproved applications. The second objective was not only to assess phase I shortcomings, as was done for fiscal year 1983 proposals, but to extend the analysis to include: I) an assessment of strengths of proposals; 2) a comparison of approved and disapproved proposals, and among approved proposals; and 3) a comparison of proposals that were funded and unfunded. The third objective was to describe for a group of phase II proposals the shortcomings and strengths articulated in their corresponding summary statements. The final objective is to provide information to the NIH extramural staff so that they may help applicants in preparing proposals by, among other things, pointing out pitfalls to be avoided in the proposal preparation process.

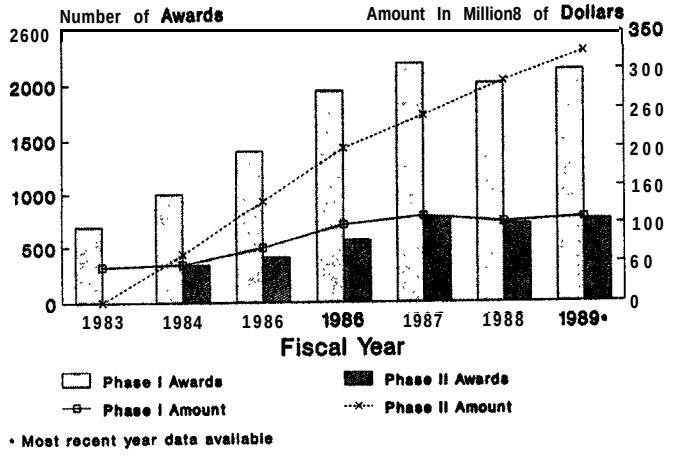

Figure 1. SBIR awards: number and amount for all Federal agencies. **Source: SBA, July 1990.**

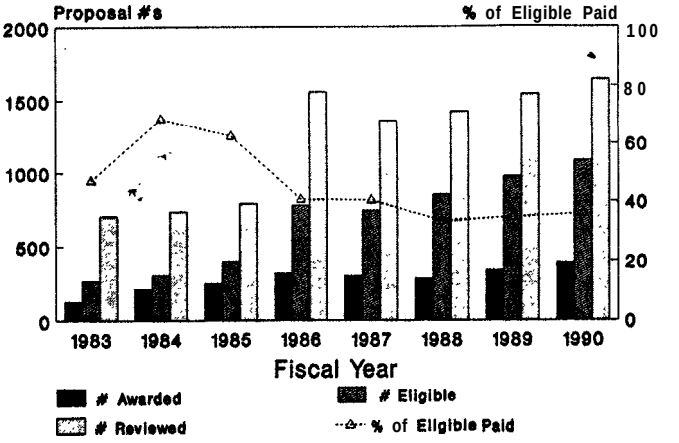

Figure 2. Phase I SBIR history (R43 Application and Award Summary), National Institutes of Health. Source: Statistical Analysis and Evaluation Section, DRG, NIH.

MATERIALS AND METHODS

Table 3 describes characteristics of the data set. Phase I applications were drawn from the October 1986 Council (N = 407) and phase II proposals were selected from the October 1986, October 1987, and January 1988 Council rounds (N = 265). For phase I applications the summary statements came from a series of ad hoc study sections convened to review SBIR proposals.

Shortcomings and strengths were divided into five different classes based on similar summary statement analyses by other investigators (4). These classes are: class I, The Nature of the Research Problem; class II, The Experimental Approach; class III, The Investigators; class IV, Requirements of the SBIR Program; and class V, Other.

Data analysis was performed using the EPIINFO software developed by the Centers for Disease Control in Atlanta. Appropriate controls were used to assess inter- and intraindividual rater variation. A logistic regression model (5) was used to determine the contributions of strengths or weaknesses to the two comparisons: disapproval vs. approval and approved-unfunded vs. approved-funded.

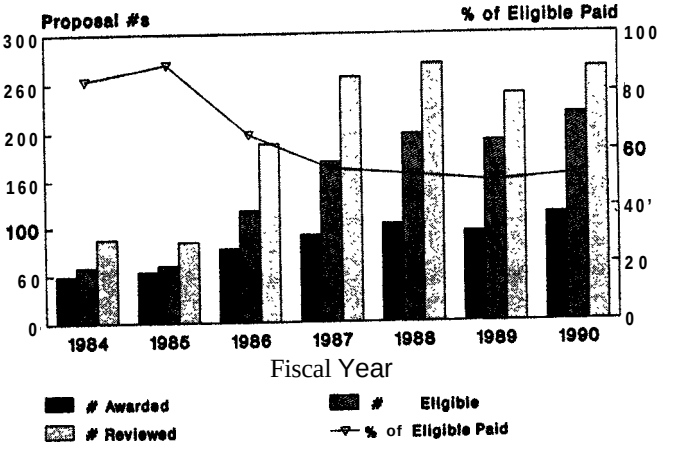

Figure 3. Phase II SBIR history (R44 Application and Award Summary), National Institutes of Health. Source: Statistical Analysis and Evaluation Section, DRG, NIH.

TABLE 1. *Examples of SBIR phase I grants"*

- Computerized nutrition program for senior citizens
- Rapid diagnostic tests for adenoviruses
- Drugs that inhibit pruritis
- Positron emission tomography for clinical use
- Anticalculus agents
- Laser fragmentation of biliary stones
- Carcinogenesis information for environmental substances
- Stereometric optic disk analysis
- Novel probes for efficient genetic disease diagnosis
- Audiovisuals for blood pressure training and testing
- Automated testing for neurological deficits
- Flow cytometry-Improving cost effectiveness

"Source: Department of Health and Human Services.

RESULTS AND DISCUSSION

Phase I data

Comparison of 1983 and 1986 data

Table 3 provides a comparison of the data published in 1985 (1983 Council actions) and the new data reported for this study (1986 Council actions) for the phase I applications. A chi-squared analysis was performed on the occurrence frequencies for each cohort for each shortcoming. A statistical difference in the relative frequencies is denoted by a triangle after the 1986 cohort column. In the first group of shortcomings (the experimental problem), without exception the frequencies of occurrence of each shortcoming were significantly greater in the 1986 cohort compared with the earlier, 1983 cohort. Within the problem category (class I) and for each cohort, shortcoming 1 (a poor hypothesis) was the most frequent observation. In the approach section (class II), the general trend is the same as in class I; that is, the proportion with class II shortcomings in the most recent study is significantly greater than in the earlier study. Exceptions to that observation are shortcomings 8 and 9 (controls and appropriate material) where significant variation did not occur. Shortcoming 5 (weakness in study design) is a prominent weakness in the second study along with shortcoming 4 (poor description of approach).

In the class III category, investigator, there was no difference in the proportion of shortcomings 11, 12, and 13 between 1983 and 1986. However, shortcoming 14 (poorly documented collaborative arrangements) was more frequent in the 1986 group. In the final class of shortcomings (SBIR requirements), the limited potential for commercial application (#15) was twice as frequent in the 1986 cohort. The frequency of shortcomings in technological innovation (#16) and the magnitude of the effort (#17) were the same in both cohorts.

Given the general trend of the comparisons in Table 3, there are several interesting points. First, in the approach section shortcoming #5 (poor study design) is significantly greater in the 1986 review results compared with the 1983 study. There are several possible explanations for differences in the results of the two studies. These include using external examiners to review the summary statements; differences in composition of the study sections; and different executive secretaries. In the investigator class of shortcomings (shortcomings 11, 12, and 13) failure to demonstrate significant differences suggests that the quality of the investigators in the 1986 group compared with the 1983 group is about the same. Under SBIR Requirements, although the potential for commercial application seems to be somewhat less in 1986 than in 1983, the technological innovation seems to have improved.

Analysis of the 1986 phase Z and the phase ZZ applications

Table 4 describes characteristics of the application data used for analysis. EPIINFO permitted subset analysis of the importance of the different variables (i.e., shortcomings and strengths) in arriving at a particular outcome (i.e., disapproval, approval-unfunded, approval-funded). Table 5 and Table 6 display those variables which significantly contributed to one of the outcomes for the approved-unfunded vs. approved-funded comparison for the phase I (Table 5) and phase II (Table 6) applications. Results of the disapproval vs. approval comparisons were similar to those of the unfunded vs. funded data. Where appropriate, differences between the comparison groups will be noted.

Table 5 reflects the S-S comparison for phase I approved-unfunded and approved-funded applications. Using a logistic regression model (with shortcomings only), the most significant shortcomings, the *absence* of which contributed to funded status, were: collaboration is needed, hypothesis is poor, lack of familiarity with the literature, unsuitable methods, poor study design, limited commercial application, and more complex than appreciated. Similarly, using a logistic regression model (with strengths only), presence of the following strengths were predictive of funding. These were: methods in place, proposal is well thought out, a need exists, and good commercial potential. The combined regression model indicates that the absence of six shortcomings are predictive of funded status (poor hypothesis, excessive complexity, unsuitable methods, collaboration is needed, lack of familiarity with the literature, and limited commercial application). Furthermore, three strengths are most predictive of being funded (methods in place, a need exists, and good commercial potential). In addition, adequate facilities *were* important in the decision between approval and disapproval.

Table 6 reflects the S-S comparisons for phase II approved-unfunded and approved-funded applications. Using a logistic regression model (with shortcomings only), the presence of four of the shortcomings were found to be predictive of unfunded status (unmet phase I objectives, poor study design, little innovation, and inadequate objectives and methods). Using a logistic regression model (with strengths only), absence of four of the strengths was found to be predictive of nonfunding. These were: defined collaborative

TABLE 2. *Examples of SBIR phase II grants'*

- Fall injury prevention system for the aged
- Control of Schistosomiasis by rotifer emissions
- Sensitive probe for intraoperative bone scanning
- A new large-scale affinity separation technique
- An acoustic body volumeter
- A periodontal temperature probe
- Pill usage chronolog and reminder
- An instrument for in vitro cytometry
- Development of tactile paper for low vision
- Correlation of dynamic molecular shape with activity
- An automated hematology microscope
- Rehabilitative software for head trauma victims

"Source: Department of Health and Human Services.

TABLE 3. *Shortcomings found* ***in disapproved SBIR, phase I proposals reviewed*** *for* ***fiscal year 1983 and 1986 action***

No.	Shortcoming	% of occurrence 1983[a]	1986[b]
	Class I: problem		
1	The proposed research is based on a hypothesis that rests on insufficient evidence, is doubtful, or is unsound	44.3	72.0"
2	The problem is more complex than the investigtaor appears to realize	15.3	39.6'
3	The problem is of insufficient importance to warrant approval	10.8	38.5'
	Class II: approach		
4	The description of the approach is too nebulous, diffuse, and lacking in clarity and technical information to permit adequate evaluation	48.6	70.3[c]
5	The overall design of the study has not been carefully thought out and developed	28.1	78.0"
6	Facilities or resources are not described or are inadequate	10.5	31.3[c]
7	The statistical aspects of the approach have not been given sufficient consideration	7.7	18.1'
8	Controls are either inadequately conceived or inadequately described	6.8	14.8
9	'The material the investigator proposes to use is unsuited to the objectives of the study	5.4	8.2
10	The proposed tests, or methods or scientific procedures are unsuited or unrelated to the stated objective	4.8	20.9'
	Class III: investigator		
11	The investigator does not have adequate experience or training, or both, for this research	44.4	37.4
12	The investigator appears to be unfamiliar with pertinent methods or literature, or both	40.6	33.0
13	The investigator needs more liaison with colleagues in this field or collateral fields	10.9	18.1
14	Collaborative arrangements are not described or not documented	8.8	19.8'
	Class IV: SBIR requirements		
15	There is limited potential for commercial application	23.0	56.6'
16	There is little technological innovation	23.0	23.6
17	The magnitude of the proposed effort is unrealistic for the amount of time allocated for phase I work	15.6	15.4
18	The cost of performing the phase I work exceeds the SBIR guidelines	6.0	0.0[c]

[a] $N = 356$. [b] $N = 182$. [c] X^2 comparison significant at < 0.05.

arrangements, well thought out, well designed, and accomplished phase I objectives. In the combined regression model the characteristics most predictive of being funded are the absence of two shortcomings (failure to achieve phase I objectives and inadequate objective and methods), and the presence of two strengths (the proposal is well thought out and it is well designed). Shortcomings related to the approaches used and the SBIR requirements dominate the results. The latter is also the case for disapproved vs. approved phase II applications.

When comparing Table 6 with Table 5, investigator difficulties seem less problematic in phase II than in phase I. As with other shortcomings and strengths, the latter is likely due to the removal of less qualified applicants during the phase I review.

SUMMARY AND CONCLUSIONS

From the preceding description and data discussion it is clear that *1*) mechanics of the SBIR program are working, and -2) a continuing effort must be made to develop the grantsmanship skills of the SBIR applicants. That the SBIR program has had a positive effect on the overall mission of the Public Health Service (PHS) was pointed out in an internal 1988 PHS report listing several positive outcomes from the PHS SBIR activity. First, the SBIR program has permitted development of instrumentation which was difficult to support under conventional or traditional grant support mechanisms. Second, SBIR activities have permitted applied research projects to proceed, providing a modicum of balance in program needs. Third, a whole new spectrum of

TABLE 4. ***SBIR*** *data set characteristics*[a]

Characteristic	Phase I		Phase II	
	Approved	Disapproved	Approved	Disapproved
Total	225	182	181	84
Number funded	90 (40%)	—	79 (44%)	—
Number amended	27 (12%)	31 (17%)	11 (6%)	25 (30%)
Bachelors (all)	19 (8%)	31 (17%)	10 (6%)	13 (16%)
Masters (all)	28 (12%)	37 (20%)	14 (7%)	9 (11%)
Ph.D.	149 (66%)	87 (48%)	117 (65%)	41 (49%)
M.D.	14 (6%)	9 (5%)	11 (9%)	8 (10%)
Other professional	5 (2%)	10 (6%)	8 (4%)	4 (5%)
No degree identified	10 (4%)	8 (4%)	21 (12%)	9 (11%)

[a] Phase I: October 1986 Council ($N = 407$); Phase II: October 1986, 1987, and January 1988 ($N = 265$).

TABLE 5. ***A listing of shortcomings and strengths contributing to funding (compared to unfunded) in phase I applications***

Shortcomings	Strengths
Poor hypothesis"	Methodologies in place"
Collaboration is needed"	Well thought out
Poor study design	Need exists'
Unsuitable methods"	Good commercial potential'
Unfamiliar with literature"	
Poor commercial potential	
Overly complex	

"Absence of these attributes (when shortcomings) or presence (when strengths) are predictive of funded status by logistic regression when shortcomings and strengths are combined in the model.

resources has been made available in both the intellectual base of the applicants and their physical facilities. Fourth, important new relationships have been developed between the SBIR applicants and the university colleagues who collaborate on many of the projects. Finally, because conventional granting mechanisms do not permit product development, the SBIR program has provided for support of development projects that may never have come to the attention of the awarding agencies.

However, an issue yet to be resolved is the suggestion that there is increasing difficulty in clinical testing of devices because of liability issues (William Partridge, personal communication). The expanding magnitude of medical products liability litigation, which results in part from a standard of absolute liability, has already forced some manufacturers to remove their products from the marketplace (6). This trend could increasingly affect grantees supported by the federal SBIR program, although it is possible that the buyout of SBIR grantees by large companies that are better able to cope with product liability issues would permit technology transfer to continue. In 1986 the National Childhood Vaccine Act (P.L. 99-660) became law. This legislation provided for the compensation of patients who experienced in adverse reaction to a vaccine product. It is conceivable that a similar program may be necessary to provide an additional measure of protection for SBIR medical device manufacturers and their clinical colleagues.

A clear result of the data presented here and that published previously (3) is that SBIR applicants need continuing assistance to improve the chances of their success. These results should serve as a guide to assist NIH staff as they provide information to prospective applicants focusing on key elements of the application. Prospective applicants are provided with some "Dos and Don'ts" to consider during the process of application in Table 7 and Table 8. A continuing review of the SBIR program would be helpful to determine if the quality of the submitted science can be improved. FJ

TABLE 6. ***A listing of shortcomings and strengths contributing*** to ***funding (compared to unfunded)*** in ***phase II applications***

Shortcomings	Strengths
Unmet phase I objectives[a]	Defined collaboration
Little innovation	Well thought out"
Poor study design	Well designed*
Inadequate methodology"	Achieved phase I objective

"Absence of these attributes (when shortcomings)-or presence (when strengths) are predictive of funded status by logistic regression when shortcomings and strengths are combined in the model.

TABLE 7. ***Dos and don'ts for phase I applicants***

Dos

- Make sure methodologies are in place
- Carefully think through your proposal and anticipate questions
- Clearly describe the available facilities and resources
- Document that a need exists
- Document the commercial potential
- Assume that you must educate and persuade the review group of the importance of your work

Don'ts

- Don't submit your application in haste.
- Don't underestimate the importance of a clearly stated hypothesis; you are submitting a research grant application.
- Don't be reluctant to state the importance of your proposal in terms of health care benefit, cost savings or scientific value.
- Don't skimp on citing up to date and relevant literature pertaining to your hypothesis and your work.
- Don't underestimate the complexity of your project.
- Don't be reluctant to seek expert consultation to bolster your project.

TABLE 8. ***Dos and Don'ts for Phase II Applicants***

Dos

- Describe how the phase I objectives were met
- Carefully think through your proposal and anticipate questions
- Clearly describe the available facilities and resources
- Spend time'carefully designing your studies.
- Assume that you must educate and persuade the review group of the importance of your work.

Don'ts

- Don't skimp on the objectives and the methods you will use to accomplish those objectives.
- Don't understate the technological innovation of your work
- Don't underestimate the complexity of your project; demonstrate that you understand the complexity and are in a position to deal with it.
- Don't submit your application in haste.

The authors would like to thank the following individuals for their technical assistance in preparing this manuscript: Mr. David Benoir, Mr. Jeff Caffey, Ms. Joan Fredericks, Dr. Francis Kendricks, Mr. Robert Moore, and Ms. Hillary Shein. The authors would also like to thank Drs. Norman Braveman, Tommy Broadwater, and Paul Parakkal and Ms. Lily Engstrom for their helpful comments. This project was supported in part by project no. NIH 88-313 from the 1% evaluation set aside.

REFERENCES

1. Anonymous. (1990) Small Business Innovation Development Act: seventh year results, Small Business Administration, Washington, D.C.
2. Murphy, D. G., and Dean, D. J. (1984) Application and review procedures for the NIH Small Business Innovation Research Program. ***Institute Insight*** March l-12
3. Vener, K. J. (1985) National Institutes of Health phase I, Small Business Innovation Research applications: fiscal year 1983 results. ***Federation Proc. 44, 2679-2684***
4. Allen, E. M. (1960) Why are research grant applications disapproved? Science 132, 1532-1534
5. Kleinbaum, D. G., Kupper, I., and Morgenstern, H. (1982) ***Epidemiologic Research.*** Lifetime Learning Publications, Belmont, California
6. Price, J. M. (1987) The liabilities and consequences of medical device development. ***J. Biomed. Materials Res.*** (Al suppl.): 35-58